

## **REMARKS**

### **Status of the claims**

Claims 1, 2 and 4-18 are currently pending in the application. Claims 1, 2 and 4-18 stand rejected. Claims 1, 5, 6, 17 and 18 are currently amended, and claim 3 is canceled. New claims 19 and 20 are added. Reconsideration and allowance of all of the pending claims is respectfully requested.

The term “a” has been cancelled from claims 1 and 17 so as to avoid the interpretation that the recited nucleic acid is a single nucleic acid. If this amendment is not acceptable, then the Examiner is requested to contact the undersigned prior to issuance of another Office Action. Further, claim 18 has been amended to correct an antecedent basis issue. These are all non-narrowing claim amendments.

New matter is not being added to the Application by way of this amendment. Support for the amendment to claim 1, and for new claims 19 and 20, may be found in original claim 3. The amendment to claims 5 and 6 correct the claim dependencies and do not change claim scope. Accordingly, entry of this amendment is respectfully requested.

### **Claim Rejections - 35 U.S.C. §103**

#### *1. Mullis in view of Nagamatsu*

At section 1, page 3, of the Office Action, claims 1, 2, 9, 12, and 14 are rejected under 35 U.S.C. §103 as being unpatentable over Mullis (U.S. Patent No. 5,187,083) in view of

Nagamatsu (U.S. Patent No. 5,032,281). For the following reasons, this rejection is respectfully traversed.

"To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." MPEP §2143.03. The Applicants respectfully submit that all of the limitations of claim 1, as currently amended, are not taught or suggested by the prior art. Neither Mullis nor Nagamatsu disclose or suggest a method for separating and purifying a nucleic acid with an organic macromolecule that comprises surface-saponified acetylcellulose. The surface-saponified acetylcellulose limitation was previously included in claim 3 (now canceled) which was not included in this rejection. Accordingly, withdrawal of this rejection is respectfully requested.

*2. Woodard in view of Nagamatsu*

At section 2, page 5, of the Office Action, claims 1, 2, 9, 10 and 12-15 are rejected under 35 U.S.C. §103 as being unpatentable over Woodard (EP 0512767) in view of Nagamatsu. For the following reasons, this rejection is respectfully traversed.

"To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." MPEP §2143.03. The Applicants respectfully assert that all of the limitations of claim 1, as currently amended, are not taught or suggested by the prior art. Neither Woodard nor Nagamatsu disclose or suggest a method for separating and purifying a nucleic acid with an organic macromolecule that comprises surface-saponified

acetylcellulose. The surface-saponified acetylcellulose limitation was previously included in claim 3 (now canceled) which was not included in this rejection. Accordingly, withdrawal of this rejection is respectfully requested.

*3. Woodard in view of Nagamatsu and Morishita*

At section 3, page 7, of the Office Action, claims 3-7 are rejected under 35 U.S.C. §103 as being unpatentable over Woodard in view of Nagamatsu and further in view of Morishita (U.S. Patent No. 4,118,336). For the following reasons, this rejection is respectfully traversed.

Claim 1, as currently amended, recites a method for separating and purifying nucleic acid from a biological sample, comprising adsorbing and desorbing nucleic acid to and from a membrane of an organic macromolecule which has a membrane thickness of 10  $\mu\text{m}$  to 500  $\mu\text{m}$ , and wherein the organic macromolecule comprises surface-saponified acetylcellulose.

Morishita discloses cellulose microcapsules with "adsorbing capacity." See Morishita, Abstract. The Examiner asserts that Morishita teaches surface saponified cellulose diacetate and triacetate particles, and that Morishita further suggests using surface saponified cellulose for the purification of nucleic acids. The Office Action cites column 9, lines 6-7; column 9, line 16; and column 10, line 7 of Morishita for support. See Office Action, page 7, line 14.

However, Morishita only briefly mentions using their saponified cellulose microcapsules to purify nucleic acids at column 9, line 7. At column 9, line 7, Morishita asserts that their microcapsules may potentially be put to various uses including:

. . . extraction and purification of antibiotics from fermentation liquids, extraction and purification of nucleic acids from the cells of microorganisms, extraction of natural dyes, recovery of valuable substances from waste liquors, decolorization, and treatment of waste liquors by removal of organic compounds.

However, the Applicants respectfully assert that this inclusion of extracting and purifying nucleic acids in a laundry list of potential uses does not provide an enabling disclosure of the subject matter of the present claims. Morishita does not provide a reasonable expectation of success in using their microcapsules in methods of separating and purifying nucleic acid from a biological sample as presently claimed. "The prior art can be modified or combined to reject claims as prima facie obvious as long as there is a reasonable expectation of success." MPEP §2143.02. "Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness." MPEP §2143.02.

The Applicants herewith submit a **Declaration** under 37 C.F.R §1.132 by Yumiko Takeshita. The Takeshita Declaration demonstrates that the cellulose microcapsules of Morishita cannot be used for separating and purifying a nucleic acid from a biological sample as presently claimed. The cellulose microcapsules in the Takeshita Declaration were prepared in the manner disclosed by Morishita (Example 12). The Takeshita Declaration shows that filtration of a solution containing plasmid DNA was impossible due to clogging, and the DNA could not be isolated. See Takeshita Declaration, page 3, last 3 lines.

Therefore, the Applicants respectfully submit that Morishita's mere mention of isolating nucleic acid in a list of varied potential uses for their capsules is inoperable, and that there is no

reasonable expectation of success of using their capsules in such methods. Morishita contains no further disclosure with regard to nucleic acid separation and isolation, and no working examples which demonstrate such a use. Since an obviousness determination requires that a reasonable expectation of success be present, this rejection cannot be maintained. See MPEP §2143.02 ("Reasonable expectation of success is required.") The Applicants respectfully submit that the rejection of claims 3-7 over Woodard in view of Nagamatsu and Morishita must be withdrawn.

*4. Woodard in view of Tam and Benjamin*

At section 4, page 8, of the Office Action, claim 11 is rejected under 35 U.S.C. §103 as being unpatentable over Woodard in view of Nagamatsu, and further in view of Benjamin (U.S. Patent No. 5,695,946). For the following reasons, this rejection is respectfully traversed.

Claim 11 is a dependent claim, which depends from claim 1. As demonstrated above, the prior art does not disclose or suggest all of the elements of claim 1. Neither Woodard, Nagamatsu, nor Benjamin disclose or suggest a method for separating and purifying nucleic acid from a biological sample comprising adsorbing and desorbing said nucleic acid to and from a membrane of an organic macromolecule wherein the organic macromolecule comprises surface-saponified acetylcellulose. Accordingly, the Applicants respectfully submit that this rejection must be withdrawn.

*5. Mullis in view of Nagamatsu and Nochumson*

At section 5, page 9, of the Office Action, claim 16 is rejected under 35 U.S.C. §103 as being unpatentable over Mullis in view of Nagamatsu, and further in view of Nochumson (U.S. Patent No. 5,552,325). For the following reasons, this rejection is respectfully traversed.

Claim 16 is also a dependent claim, which ultimately depends from claim 1. As demonstrated above, the prior art does not disclose or suggest all of the elements of claim 1. Neither Mullis, Nagamatsu, nor Nochumson disclose or suggest a method for separating and purifying nucleic acid from a biological sample comprising adsorbing and desorbing said nucleic acid to and from a membrane of an organic macromolecule wherein the organic macromolecule comprises surface-saponified acetylcellulose. Accordingly, the Applicants respectfully submit that this rejection must be withdrawn.

*6. Mullis in view of Nagamatsu, Nochumson, and Heath*

At section 6, page 11, of the Office Action, claims 17 and 18 are rejected under 35 U.S.C. §103 as being unpatentable over Mullis in view of Nagamatsu, and further in view of Nochumson and Heath (U.S. Patent No. WO 99/13976). For the following reasons, this rejection is respectfully traversed.

As demonstrated above, the prior art does not disclose or suggest all of the elements of the present claims. Neither Mullis, Nagamatsu, nor Nochumson disclose or suggest a method for

separating and purifying nucleic acid from a biological sample as presently claimed.

Accordingly, the Applicants respectfully submit that this rejection must be withdrawn.

### **Double Patenting Rejections**

At page 12 of the Office Action, claims 1, 2 and 4-18 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 1-2 of copending application 10/305,110 and claims 1-18 of copending application number 10/621,412; and claims 1-20 of copending application number 10/621,715 in view of Tam (U.S. Patent No. 5,741,647). This rejection is respectfully traversed.

The applicants respectfully refer the Examiner to the MPEP 804, page 800-17, the relevant section of which is provided below:

If a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer. If the ODP rejection is the only rejection remaining in the later-filed application, while the earlier-filed application is rejectable on other grounds, a terminal disclaimer must be required in the later-filed application before the rejection can be withdrawn.

### **Conclusion**

An early reconsideration and Notice of Allowance for pending claims 1, 2 and 4-18 is respectfully requested. Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark Konieczny (Reg. No. 47,715) at the telephone number below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Dated: September 22, 2006

Respectfully submitted,

By 

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Attachment:

*J.M.K.*

DECLARATION UNDER 37 CFR 1.132

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: :  
Toshihiro Mori, et al. : Group Art Unit: 1637  
Appln. No.: 10/621,329 : Examiner: BABIC, CHRISTOPHER M  
Filed: July 18, 2003 :  
For: A METHOD FOR SEPARATONG AND PURIFYING A NUCLEIC ACID

DECLARATION UNDER 37 C.F.R. §1.132

Assistant Commissioner for Patents  
Alexandria, VA 22313-1450

Sir:

I, Yumiko TAKESHITA of 11-46, Senzui 3-chome, Asaka-shi, Saitama, Japan, hereby declare and state that I received a Bachelor degree of Chemical and Biological Sciences from Japan Woman's University on March 1989 and that I have been employed as a worker in research by Fuji Photo Film Co. Ltd. since April 1989.

I declare that I am at present doing research work on nucleic acid extraction and detection in Life Science Research Laboratory of said company.

I am familiar with the subject matter disclosed by the application.

The following experimentation was conducted by me.

**Preparation of Cellulose Microcapsule**

A cellulose microcapsule was prepared in the same manner as in Example 12 of U.S. Patent No. 4,118,336 (Morishita) except for reducing a scale to 1/4. Specially, 10 g of bentonite powder was added to a solution of 2.5 g of cellulose triacetate in 50 ml of methylene chloride and was dispersed. The resulting dispersion was dispersed with propeller stirring to the form of fine droplets into 200 ml of an aqueous solution containing 1 g of sodium laurylbenzene sulfonate dissolved herein. After the methylene chloride was removed by an evaporator to form microcapsules, the microcapsules formed was tried to be filtered, but a clogging of the filter occurred completely. Due to the clogging, various filters such as a glass filter and paper filter were tried, but even in all of the filters, a clogging occurred. Thus, a precipitate was separated, and the remaining was freeze-dried. To the precipitate and the freeze-dried product were added 30 ml of water to be washed three times (a centrifugation with 1500 rpm for 10 minutes and removal of the supernatant was performed three times) to obtain microcapsules encapsulated with cellulose triacetate containing bentonite powder. Subsequently, 10 g of the microcapsules were swelled for 30 minutes in 6 ml of a mixture of ethanol and water (1:1), and then the supernatant was removed by a centrifugation. The pellet was charged into 6 ml of 0.5 N sodium hydroxide and saponified with stirring at 50°C for 30 minutes. Thereafter, the microcapsules was washed with water three times and then cellulose microcapsule was obtained.

The separation and purification of a plasmid DNA from a recombinant bacterium was performed by using the cellulose microcapsule obtained above.

**Preparation of Solution containing a plasmid DNA**

A frozen recombinant bacterium containing a plasmid: pBlueScript II/GAPDH/DH5 $\alpha$  was thawed at a room temperature, and then the thawed recombinant bacterium was subjected to a tapping of ten times. To the tapped material was added 100  $\mu$ l of RDP dispersion (50mM TrisHCl and 10mM EDTA: pH 8.1) containing 3  $\mu$ l of EDP-A solution (0.3 mg/ml of RNase A and 0.27 mM of sodium acetate) and 1  $\mu$ l of EDP-B solution (0.01 mg/ml of RNase T1 and 32 mM of ammonium sulfate). After the solution was vortexed at a maximum speed for 15 seconds, to the vortexed solution was added 100  $\mu$ l of ADP solution (0.2N sodium hydroxide and 1% SDS: pH 13). Immediately after the addition of ADP, an inversion mixture was slowly performed five times. To the obtained solution was added 140  $\mu$ l of NDP solution (3M potassium acetate and 13.6% acetic acid: pH 5.5). Immediately after the addition of NDP, an inversion mixture was slowly performed five times. The obtained solution was then centrifuged at 18,000g for 10 minutes at room temperature, and then the supernatant was isolated as a solution containing a plasmid DNA (approximately 330  $\mu$ l).

**Isolation of Plasmid DNA**

(1) To 1.7 ml of tube, 70 mg of the cellulose microcapsule obtained above, 320  $\mu$ l of LDP solution (31.3 mM Bis-Tris and 7.1% Tween 20 in 68.5% of ethanol: pH 6.0) and the solution containing a plasmid DNA (approximately 330  $\mu$ l) were added. The obtained solution was subjected to vortexing at a maximum speed for 30 minutes, and then was subjected to a filtration by a glass filter. However, the filtration was impossible due to a clogging, and the plasmid DNA was not able to be isolated.

On the contrary, the method of the present invention can isolate the plasmid DNA by the above-mentioned operation.

(2) Instead to the above operation, the whole solution containing a plasmid DNA (approximately 330  $\mu$ l) after several-time pipetting was added to a tube containing 70 mg of the cellulose microcapsule obtained above. The obtained solution was subjected to vortexing for one minute and centrifuging at 1,000g for one minute, and the supernatant was removed. To the pellet, 750  $\mu$ l of a washing solution (10.8 mM TrisHCl in 80% of ethanol: pH 7.8) was added. The obtained solution was subjected to vortexing for one minute and centrifuging at 1,000g for one minute, and the supernatant was removed. To the pellet, 750  $\mu$ l of the washing solution was added. The obtained solution was subjected to vortexing for one minute and centrifuging at 1,000g for one minute, and the supernatant was removed. To the pellet, 50  $\mu$ l of a recovering solution (10 mM TrisHCl: pH 8.5) was added, and then the obtained solution was subjected to vortexing for one minute and centrifuging at 1,000g for one minute to obtain the plasmid.

Although a plasmid DNA can be isolated by many further operations in Morishita, the many further operations are an extremely troublesome. Accordingly, from the above result, it can be recognized that the method of the present invention at least has an excellent separation performance.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or

both, under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectively submitted,

Date: 09/21/06

Yumiko Takeshita

Yumiko TAKESHITA